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EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 07/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/807,657	GARCON, NATHALIE	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *See Continuation Sheet* is/are allowed.

6)☒ Claim(s) *39,41,49,59,89,100,104,108,110-114,120-122 and 134* is/are rejected.

7)☒ Claim(s) *40,86,91,92 and 127* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 April 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 39-42,46,48-53,56,58-62,71,75,77,78,82,86,88-93,97,99-104,108,110-114,116,120-125,127,131,133 and 134.

Continuation of Disposition of Claims: Claims allowed are 42,46,48, 50-53,55,56,58, 60-62,71,75,77,78,82,88, 90, 93,97,99, 101-103,123-125,131, and133

DETAILED ACTION

Status of the Claims

1. Claims 32-37, 39-42, 46, 48-53, 56, 58-62, 71, 73-82, 84-86, 88-93, 95-97, 99-104, 106-116, 120-125, 127, 131, and 133-141 were pending in the prior action mailed on October 19, 2006. In that action, claims 39-42, 46, 48-53, 56, 58-62, 71, 75, 77, 78, 82, 86, 88-93, 97, 99-104, 108, 110-114, 116, 120-125, 127, 131, 133, and 134 were indicated to be allowable; and claims

32-37, 73, 74, 76, 79-81, 84, 85, 95, 96, 106, 107, 109, 115, and 135-141 were rejected.

2. The Applicant submitted a Response on April 19, 2006. In the Response, the Applicant amended claim 50; and cancelled claims 32-37, 73, 74, 76, 79-81, 84, 85, 95, 96, 106, 107, 109, 115, and 135-141.

3. Claims 39-42, 46, 48-53, 56, 58-62, 71, 75, 77, 78, 82, 86, 88-93, 97, 99-104, 108, 110-114, 116, 120-125, 127, 131, 133, and 134 are currently pending.

4. In view of the new rejections presented below, the action is made Non-Final.

Allowable Subject Matter

5. The subject matter of claims 42,46,48, 50-53,55,56,58, 60-62,71,75,77,78,82,88, 90, 93,97,99, 101-103,123-125,131, and133 are allowed for the reasons indicated in the prior action.

Specification

6. **(Prior Objection- Withdrawn)** The specification is objected to for containing referring to sequences without also identifying them by the sequence identifier assigned to them in the sequence listing as required by 37 CFR 1.821(d). See e.g., p. 6, lines 30-32.In view of the amendment to the specification, the objection is withdrawn.

Claim Objections

7. **(Prior Objection-Withdrawn)** Claim 140 was objected to because of the following informalities: the claim refers to polynucleotide sequences without also referring to them by the appropriate SEQ ID NOs as required under 37 CFR 1.821(d). In view of the cancellation of the claim, the objection is withdrawn.

8. **(New Objections)** Claims 86, 91, 92, 127 objected to because of the following informalities:

In claim 86, the hyphen before the term "of" in line 1 of the claim should be deleted.

In claims 91 and 92, respectively, there should be a space between the term "claim" and the terms "51" or "52."

In claim 127, the hyphen above the comma in line 1 should be deleted.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. **(Prior Rejection- Withdrawn)** Certain claims were rejected under 35 U.S.C. 112, second paragraph, as being indefinite as depending, directly or indirectly, from canceled claims 44, 45, 55, 129, and 130. In view of the cancellation or amendment of such claims, the rejection is withdrawn.

11. **(New Rejection)** Claims 104, 108, and 110-114 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims are drawn to methods comprising the use of "safe and effective" vaccines. These claims are rejected because it is not clear what is being claimed.

These claims are rejected in part because it is not clear what the Applicant means through use of the "safe" language. For example, it is known in the art that several therapeutic compositions (e.g. Botulinum toxin, certain anti-viral and anti-bacterial drugs) are known to have negative impacts on organisms to which they are administered, but that in certain circumstances the toxic effects of such compounds are considered secondary to their therapeutic effects. The term "safe" is therefore a relative term which renders the claim indefinite. As the application does not provide a standard for ascertaining the requisite degree, one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is additionally noted that it is not within the purview of the USPTO to determine the safety of a claimed invention. It is therefore suggested that the term "safe" be deleted from the claims.

The claims are also rejected because it is not clear what the "effective amounts" are effective for. See e.g., MPEP § 2173.05(c) III. It is therefore suggested that the term "effective" also be deleted from the claims, or that the claims be amended to identify what the "effect amount" is effective for.

12. **(New Rejection)** Claims 49, 59, 89, 100, 111, 134 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims read on compositions comprising a first and a second complex, wherein the second complex comprises a plurality of subcomplexes, each subcomplex comprising an antigen adsorbed onto a metallic salt particle and wherein each subcomplex comprises a different antigen. The claims are rejected because it is not clear what is meant by the requirement that the second complex comprises of a plurality of subcomplexes. I.e., it is not clear if the claims are intended to require that each of the subcomplexes are complexed one with the others, or if the Applicant intended to describe compositions comprising a first population of complexes and a second population of complexes, wherein the second population of complexes comprises a plurality of subpopulations of complexes as described above.

Clarification is required.

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. **(New Rejection)** Claims 104, 108, and 110-114 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. These claims are drawn to method for treating an animal suffering from cancer comprising the administration of a vaccine composition.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. Id. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered. In the present case, those factors considered most relevant are the presence or absence of working examples, the state of the prior art, the predictability in the art, and the breadth of the claims.

As indicated above, the rejected claims are directed to methods for the treatment of cancers comprising the administration of a vaccine composition. However, the application provides no demonstration of therapeutic efficacy of any vaccine for the treatment of a cancer. Rather, while the application identifies certain potential cancer antigens that were known in the

art as potential anti-cancer vaccine antigens (pages 12-13), the only examples of antigens provided in the application are anti-pathogen (and more specifically, anti-viral) antigens.

The surrounding the therapeutic vaccination for treatment of cancers indicates that, while there is cause for hope in the development of anti-cancer vaccines, as yet "clinical results achieved with cancer vaccines is limited, and no vaccination regimen is currently recommended." See e.g., Mocellin et al., Exp Cell Res 299: 267-78, at 273-74. See also, Stevenson, Curr Opin Oncol 17: 573-77, at 573 (indicating that whereas vaccines that inhibit formation of viral associated tumors have been developed, as of 2005 there was still significant uncertainty in the development of therapeutic vaccines against cancers). The art identifies several basis for uncertainty in the operability of such vaccines, and indicates that the immune-related mechanisms of cancers is still not fully understood. See e.g., Mocellin, at 268 (tumor immune escape), 269 (suitable targets/antigens), 271 (indicating variability in the use of different adjuvants), and 273-74. Thus, the art indicates that at the time that the present application was filed, while certain antigens were known in the art, their use as anti-cancer vaccines had not been demonstrated, and remains uncertain. The art further identifies several ground of unpredictability in the art.

In view of the limited guidance and lack of working examples in the present application for the use of therapeutic anti-cancer vaccines, and the teachings in the art relating the complexity, unpredictability, and relatively undeveloped state of the art, the disclosure of the present application does not enable those skilled in the art to practice the claimed inventions without undue experimentation.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. **(Prior Rejection- Expanded)** Claims 32-37, 115, 138, and 139 were rejected under 35 U.S.C. 102(b) as being anticipated by EP 0 576 478 (of record in the September 29, 2005 IDS). These claims have been cancelled from the application. The rejection is therefore withdrawn from these claims.

However, it is noted that claims 39 and 41 read on processes for the making of immunogenic compositions comprising the admixing of an adjuvant composition containing an immunostimulant adsorbed onto a first metallic salt particle, and an antigen. While the claims require that the metallic salt onto which the immunostimulant is adsorbed is substantially free of antigen prior to the admixing, there is no requirement that, in the resulting immunogenic composition, the metallic salts remain substantially free of the antigen. Nor does any step in the claimed process for the admixing inherently result in compositions wherein the salt remains substantially antigen free. As the reference teaches a process for combining an HSV antigen with an adjuvant composition as described (see e.g., page 3), the reference anticipates the indicated claims.

It is noted that the rejection is not extended to claim 40, which requires that the antigen is adsorbed onto a second, separate, metallic salt from the metallic salts used in the adjuvant compositions.

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. **(Prior Rejection- Withdrawn)** Claims 138-141 were rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0 576 478 as applied to claims 32-37, 115, 138, and 139 above, and further in view of the Applicant's admission on pages 1, 5-6 of the application that vaccine compositions comprising the indicated immunostimulants were known in the art and of the Vogel et al. reference cited in the September 2005 IDS. In view of the cancellation of the indicated claims, the rejection is withdrawn.

19. **(New Rejection)** Claim 120 is rejected under 35 U.S.C. 103(a) as being unpatentable LaPoste et al. (U.S. 6,306,404) over EP 0 576 478 (as applied to claims 39 and 41 above. This claim is drawn to the process of claim 41, wherein the antigen is an anti-HPV antigen.

LaPoste teaches the use of the 3D-MPL adjuvant to improve the immune responses against antigens from HPV. See e.g., claims 7 and 9. However, the reference does not teach a

method for making compositions comprising the HPV antigen and 3D-MPL as described in the present claims.

The teachings of EP 0 576 478 have been described above. This reference does not teach the making of an immunogenic composition comprising an anti-HPV antigen.

However, because both references relate to the making and use of compositions comprising 3d-MPLas an adjuvant for an antigen, it would have been obvious to those in the art to use the method of the EP reference to make the HPV/3D-MPL compositions described by LaPoste. This is because those of ordinary skill in the art would have recognized that the methods of the two references for the making of the compositions disclosed therein were functional equivalents one of the other. The combined teachings of these references therefore render the claimed inventions obvious.

20. **(New Rejection)** Claims 121 and 122 are rejected under 35 U.S.C. 103(a) as being unpatentable over LaPoste in view of EP 0 576 478as applied to claim 120 above, and further in view of Rose et al. (J Virol 72: 6151-54). These claims read on the method of making an immunogenic composition of claim 41, wherein the antigen is an HPV antigen, particularly from one of HPV 6, 11, 16, or 18, and wherein the antigen is an L1 particle or a capsomer. The teachings of the LaPoste and the EP reference have been described above. While the combination of LaPoste and the EP reference render obvious embodiments of the claimed method wherein the antigen is from HPV, they do not specify the limitations of claims 121 and 122.

However, Rose teaches HPV 11 antigens comprising a capsomer (an L1 particle) which is able to induce neutralizing HPV antibodies. It would therefore have been obvious to those of ordinary skill in the art to use such antigens in the anti-HPV composition suggested by LaPoste. This is because it would have been apparent to those of ordinary skill in the art that the HPV antigens of Rose were functional equivalents for the generic HPV antigens of LaPoste. Thus, the combined teachings of Rose with those of LaPoste and the EP reference render the claimed methods obvious.

Conclusion

21. Claim 40 is objected to as dependent from a rejected claim.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas 7/5/06
Patent Examiner